Decreased Testosterone in the Aging Male

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Supplement Editor, *Decreased Testosterone in the Aging Male*
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[Rev Urol. *2003;5(suppl 1):S1–S2*]

Testosterone deficiency in the aging male is associated with the loss of libido, erectile dysfunction, depression, decreased cognitive ability, lethargy, osteoporosis, and loss of muscle mass and strength. This constellation of symptoms is known collectively as andropause, or ADAM (androgen deficiency of the aging male), and the syndrome is likely to become more common as the baby-boomer generation continues to grow older.

Androgen replacement therapy, which focuses on replacing lowered androgen levels with exogenous androgens, can safely alleviate the detrimental effects of decreasing androgen levels in aging men. This compendium of seven lectures, presented during a symposium held on July 20–21, 2002, in Seattle, Washington, presents the latest thinking on diagnosing and treating andropause; describes the role of therapies, such as oral, intramuscular injections, patches, and testosterone gels; and discusses the potential risks associated with treatment.

Dr. Alvin M. Matsumoto, in his review of the fundamental scientific aspects of androgen deficiency in aging men, describes the loss of serum testosterone as an age-related physiologic change—as men grow older, their testosterone levels decline. This decline in testosterone can be attributed to diminished testicular production of testosterone and reduced hypothalamic secretion of gonadotropin-releasing hormone, which results in inadequate luteinizing hormone secretion by the pituitary gland. Dr. Matsumoto explains that androgen replacement therapy's most decided role is in treating patients with consistently low testosterone levels and symptoms consistent with andropause. Treatment in these patients may beneficially affect body composition, bone mineral density, angina, exercise-induced ischemia, and other androgen-regulated physiologic functions. He also emphasizes that alterations in physiologic functions are often attributable to multiple etiologic causes such as poor nutrition, illnesses, medications, inactivity, and excessive alcohol con-

sumption. Addressing these sources of physiologic change is equally as important as addressing testosterone deficiency itself.

But who are the potential candidates for treatment, and how can clinicians best evaluate these candidates and the success of treatment? Dr. Michael P. O'Leary summarizes the two diagnostic tools currently available for evaluating men with low testosterone levels and the steps that still need to be taken to develop a reproducible methodology for diagnosis. The tools—two questionnaires—in clinical use today have not undergone vigorous psychometric testing, Dr. O'Leary explains. As more men present with androgen deficiencies, thoroughly validated diagnostic and quality-of-life instruments will be necessary to accurately screen patients and monitor therapeutic responses.

In addition to the multiple etiologic causes of andropause, presentation may vary from patient to patient, making accurate diagnosis a challenge. There are six clinical changes, described by Dr. Jeremy P.W. Heaton, that should alert physicians to the possibility of androgen deficiency: decreased sexual desire and erectile quality, decreased intellectual capacity, decreased lean body mass, body hair and skin changes, decreased bone mineral density, and increased visceral fat. Importantly, Dr. Heaton correlates each of these symptoms with the hormone believed to be responsible. Testosterone, leptin, estradiol, cortisol, prolactin, thyroxine, growth hormone, and dehydroepiandrosterone are all believed to play a role in andropause.

Several androgen replacement therapies are available for the treatment of andropause. Dr. J. Lisa Tenover reviews these therapies, which include oral preparations, intramuscular injections, patches, and gels. Dr. Tenover covers the potential benefits and adverse events associated with each product, how to choose an agent for a particular patient, and how to measure effectiveness. Efficacy of treatment is typically measured by increases in serum testosterone levels, explains Dr. Tenover, and physicians need to keep vigilant watch for complications such as worsening sleep apnea, a worsening cardiovascular risk profile, and gynecomastia. Patients also need to be monitored for administration-related complications (pain at injection site or local skin irritation).

As with any therapy, safety is of paramount concern. The safety of androgen replacement is addressed in this supplement by Dr. Michael K. Brawer. The major issue surrounding androgen replacement therapy is its potential role in prostate carcinogenesis. Dr. Brawer points out that the relationship between serum hormone levels and prostate cancer has yet to be conclusively elucidated, and that there is no evidence that androgen supplementation increases the risk of cancer. However, androgen replacement therapy does promote the growth of already existing carcinomas, necessitating that patients undergo careful screening for malignancy prior to treatment and careful monitoring while undergoing treatment. With these measures in place, androgen supplementation is a safe treatment for hormonal deficiency in aging men.

The newest treatment for androgen deficiency is the testosterone supplement Testim™ (Auxilium Pharmaceuticals, Inc., Norristown, PA), a topical gel. Dr. Christopher P. Steidle reviews the pharmacokinetics and clinical data of this agent. Testim provides consistent transdermal absorption of testosterone for 24 hours following a single dose and produces higher serum testosterone levels than other marketed gel formulations. Its safety profile is similar to that of the other available agents, and it does not increase the risk of prostate cancer.

To help further elucidate the diagnostic process, the factors that must be considered, and the decisions that must be made when prescribing treatment, Dr. Andrew McCullough presents three cases studies. The patients—a 66-year-old man with partial androgen deficiency syndrome, a 42-year-old man with testosterone deficiency following bilateral orchiectomy for metachronous seminoma, and a 58-year-old man with sildenafil-refractory erectile dysfunction following treatment for localized prostate cancer—are typical of those who might present to a urologist for treatment of the symptoms associated with androgen deficiency.

As the elderly population increases, so, too, will the incidence of testosterone deficiency, and the opportunities for urologists to improve patients' lives through androgen replacement therapy. This collection of articles presents the latest thinking and data on diagnosing and treating this syndrome. ■